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Tangstophosphoric acid ($H_3PW_{12}O_{40}$): An efficient and eco-friendly catalyst for the one-pot synthesis of dihydropyrimidin-2(1*H*)-ones

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Abstract

Tangstophosphoric acid both in bulk form or supported on silica gel efficiently catalyzed the three-component condensation reaction of aldehyde, 1,3-dicarbonyl compound and urea or thiourea to afford the corresponding 3,4-dihydropyrimidin-2(1*H*)-ones in high yields under solvent-free conditions at 80 °C. This catalyst is efficient not only for open chained β-dicarbonyl compounds, but for the cyclic β-diketones, β-diester or β-diamide derivatives such as dimedone, Meldrum's acid or barbituric acid derivatives.

Keywords: Heteropolyacid; Tangstophosphoric acid; Dihydropyrimidinones; Biginelli reaction; Solvent-free

1. Introduction

The dihydropyrimidinone ring system is contained within a number of pharmacologically active agents [1], for example, calcium channel blockers, antihypertensive agents, α-1a-antagonists, antiviral, antitumor and anti-inflammatory drugs [2], they have been subject of extensive investigations. In addition, the 2-oxodihydropyrimidine-5-carboxylate core unit is found in nature and in potent HIVgp-120-CD_4 inhibitors [3].

Synthetic strategies for the dihydropyrimidinone derivatives would involve one-pot to multistep approaches [1]. The first one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones was reported by Biginelli in 1893, often involves unsatisfactory yields (20–60%), harsh reaction conditions and long reaction times [4,5]. Although high yields could be achieved by complex multi-step synthesis procedures, these methods lack the simplicity of the original one-pot Biginelli protocol [6]. Therefore, in recent years interest in this reaction has increased rapidly and several modifications and improvements using Lewis acids as well as protic acid under classical reflux [7–13], solvent-free conditions [14–18] and microwave [19–23] or ultrasound irradiation [24,25] have been reported.

However, in spite of their potential utility, many of these methods involve expensive reagents, strong acidic conditions, long reaction times, high temperatures, stoichiometric amount of catalysts, environmental pollution and give unsatisfactory yields. Therefore, to avoid these limitations, the discovery of a new and efficient catalyst with high catalytic activity, short reaction time, recyclability and simple work-up for the preparation of 3,4-dihydropyrimidin-2(1*H*)-ones under neutral, mild and practical conditions is of prime interest. Due to the super acidic properties of solid heteropolyacids (HPAs), in the last three decades, heteropolyacids have found numerous applications as useful and versatile acid catalysts for some acid-catalyzed reactions [26]. They are usually solids that are insoluble in non-polar solvents but highly soluble in polar ones. They can be used in bulk or supported forms in both homogeneous and heterogeneous system. Furthermore, hetero-

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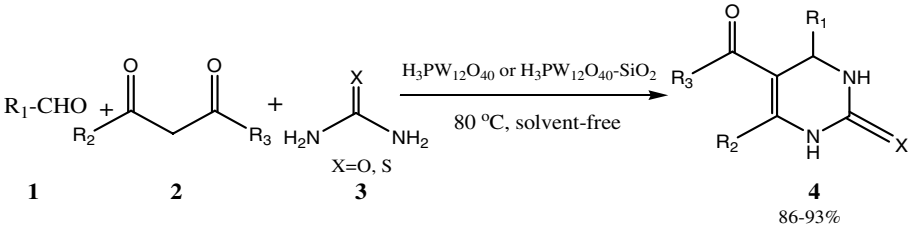
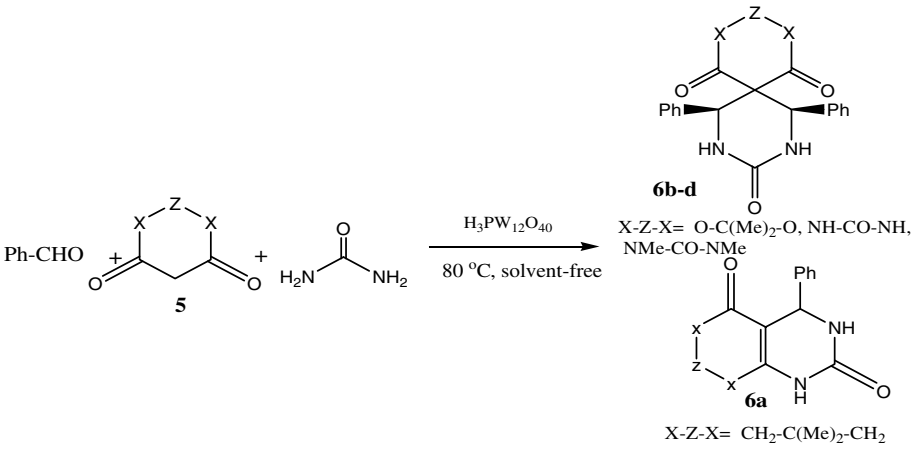


Scheme 1.



Scheme 2.

polyacids have several advantages, including high flexibility in modification of the acid strength, ease of handling, environmental compatibility, non-toxicity, and experimental simplicity [26].

In continuation of our interest on the Biginelli and Biginelli-like reactions [27], we wish to report a simple, efficient and practical approach for the Biginelli reaction using tangstophosphoric acid or silica gel supported tangstophosphoric acid as eco-friendly catalyst with high catalytic activity under solvent-free conditions at 80 °C (Scheme 1). This catalyst is efficient not only for open chained β-dicarbonyl compounds, but also it is proper for cyclic β-diketones, β-diester or β-diamide derivatives such as dimedone, Meldrum's acid or barbituric acid derivatives (Scheme 2).

2. Experimental

2.1. Materials and methods

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DRX-500 AVANCE spectrometer at 500.13 and 125.77 MHz, respectively. NMR spectra were obtained on solutions in DMSO-d_6. The chemicals used in this work were purchased from Fluka (Buchs, Switzerland) chemical company. Tangstophosphoric acid ($H_3PW_{12}O_{40}$) was prepared according to a reported procedure [26c].

2.2. Preparation of the silica gel supported tangstophosphoric acid

The silica gel supported tangstophosphoric acid was prepared by mixing silica gel (1.50 g, Merck grade 60, 230–400 mesh) with a solution of tangstophosphoric acid (0.50 g) in distilled water (10 ml). The resulting mixture was stirred for 30 min and then water was removed in a rotary evaporator and the solid powder was dried at 70 °C for 3 h.

2.3. General procedure

2.3.1. Tangstophosphoric acid catalyzed synthesis of dihydropyrimidinones

A mixture of aldehyde (1 mmol), 1,3-dicarbonyl compound (1 mmol), urea or thiourea (1.5 mmol, 0.09 g) and tangstophosphoric acid (2% mmol, ca. 0.06 g) was heated with stirring at 80 °C for an appropriate time (TLC). After cooling, the reaction mixture was washed with cold water and residue recrystallized from ethyl acetate–hexane (1:3) to afford the pure product.

2.3.2. Silica gel supported tangstophosphoric acid catalyzed synthesis of dihydropyrimidinones

A mixture of aldehyde (1 mmol), 1,3-dicarbonyl compound (1 mmol), urea or thiourea (1.2 mmol, 0.07 g) and